Amendments to the Drawings:

The attached drawing includes changes to Figure 1A. In Figure 1A a sequence identifier was provided for the LPXTG motif and amino acid # 639 was changed to # 609.

Attachment: Replacement Sheet

Remarks/Arguments

Applicants thank the examiner for discussing the application in an in person interview on February 24, 2009. During the interview, the rejections of record were discussed. The discussions included reference to "comprises" and "consists" as provided in claims 2 and 3; and Foster et al. (US 6,841,154). Also discussed during the interview was percent identity language.

The present amendment without prejudice to future prosecution: amends claims 1, 3-8, and 33-46; cancels claims 2, 10, 17, 18, 20, 21, 24, 25, 27, and 29; adds new claims 47-54; amends the specification; and provides a replacement for Figure 1A. Cancelled claims 10, 17, 18, 20, 21, 24, 25, 27, and 29 were previously withdrawn from consideration for being directed to a non-elected invention.

Claim 1 was amended to reference "purified", and incorporate the description previously provided in claim 2, along with a clarification to the claim 2 language. Support for reference to purified is provided in the application on page 14, lines 18-30.

Claim 2 was previously indicated to be confusing based on its employing open and closed ended language. Open and closed ended language was employed to provide an upper limit of "consisting" of a sequence at least 90% identical to SEQ ID NO: 3 and a lower limit based on a fragment of SEQ ID NO: 3. The fragment contains a sequence at least 90% identical to SEQ ID NO: 1. SEQ ID NO: 1 corresponds to the ORF0657nl region, which is a portion of SEQ ID NO: 3. (See, for example, Figure 1A and Table 1 on page 8.)

The clarification to the claim 2 description is intended to more clearly indicate that reference to "comprising" with respect to a "fragment" allows for a SEQ ID NO: 1 related region that has an upper limit at least 90 % identical to SEQ ID NO: 3. Reference to a fragment indicates less that the SEQ ID NO: 3 description.

A similar clarification was provided with respect to claim 3, indicating at least 94 % identity. The clarification to the claim 2 and 3 descriptions is not intended to alter the scope of descriptions provided in original claims 2 and 3.

Reference to either (a) an amino acid sequence at least 90% identical to SEQ ID NO: 3, or (b) a fragment of said amino acid sequence at least 90% identical to SEQ ID NO: 3, where said fragment comprises an amino acid sequence at least 90% identical to SEQ ID NO: 1 is supported by original claim 2. In addition, Figures 2A-2E illustrate support for the at least 90%

identity. Figures 2A-2E provide a sequence comparison for different *S. aureus* sequences across the ORF0657nH region, which includes the ORF0657nI region.

The ORF0657nI region in Figures 2A-2E goes from amino acid 3 to amino acid 455 and illustrates examples of differences between SEQ ID NO: 1 and different naturally occurring sequences. Adding the total differences between SEQ ID NO: 1 and at least one of the other strains provides for 49 differences. The 49 differences are arrived at by adding the 46 differences noted in bold in Figures 2A-2E along with 3 amino acids at positions 63-65 (see for example, ID15).

Dividing 49 by the overall size of SEQ ID NO: 1 (446 amino acids) provides a sequence identity of 89%, which supports at least 90% sequence identity.[1] Figures 2A-2E illustrate a higher percentage of amino acid differences in the region after ORF0657nI.

Figures 4A-4H further support the ability of a polypeptide containing a region related to SEQ ID NO: 1 to provide protective immunity. Figures 4A-4H illustrate the ability of SEQ ID NO: 28 to provide protection against different heterologous clinical isolates designated CL-10, CL-13, CL-30, CL-18 and CL 21. SEQ ID NO: 28 corresponds to SEQ ID NO: 2 with a His-Tag. (The present application at page 9, Table 1). CL-10, CL-13, CL-30, CL-18 and CL 21 are diverse *S. aureus* strains with different sequence identity to SEQ ID NO: 2. (The present application at pages 28 and 29, Table 3.) With respect to the Figures 2A-2E sequence alignment: CL-10 corresponds to ID11, CL-13 corresponds to ID19, CL-18 corresponds to ID-18, CL-21 responds to ID-22, and CL30 corresponds to ID24.

It is respectfully submitted that the ability of full-length ORF0657n of SEQ ID NO: 2 to provide protective immunity, along with Figures 2A-2E sequence comparison, indicates that variations within SEQ ID NO: 1 could be made and still retain the ability to provide protective immunity. Such an expectation is based on SEQ ID NO: 1 being sufficient to generate a protective immune response and the ability of the longer-length sequence (SEQ ID NO: 28),

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[1] The 446 amino acids used in the calculation is for the full-length SEQ ID NO: 1, which includes an amino terminal methionine. The sequence alignment provided in Figures 2A-2E does not show the amino acid corresponding to the SEQ ID NO: 1 amino terminus methionine for all the sequences. The presence of an amino acid other than methionine in the corresponding position would lower the sequence identity.

which contains SEQ ID NO: 1, to provide protection against heterologous strains with different sequences. For example, based on Figures 4A-4H, the corresponding SEQ ID NO: 1 region from CL-10, CL-13, CL-30, CL-18 and CL 21 would at least be expected to provide protection against the homologous strain.

Claims 4 and 33-36 were amended to refer to "polypeptide" as a "polypeptide immunogen".

Claim 5 was amended to provide an independent claim format and replace "consisting essentially". Consisting essentially was replaced with consisting of a particular sequence with up to 20 additional amino acids, wherein the additional 20 amino acids can be located at the carboxyl or amino terminus. Support for up to 20 additional amino acids is provided in the application on page 13, lines 14-19.

Claim 7 was amended to indicate the immunogen consists of an amino acid sequence at least 90% identical to SEQ ID NO: 1 and one or more additional regions, and to clarify reference to regions or moieties. The application on page 3, lines 5-7 excludes from the additional region or moiety sequence related to ORF0657n. Thus, claim 7 would not provide the full-length ORF0657n polypeptide.

Claim 8 was amended to describe an independent composition claim directly providing the polypeptide immunogen description of claim 1, and in the claim preamble indicating the protective immune response is against *S. aureus*. Claim 8 previously referred to the immunogen of claim 1.

Claims 37, 39, 41, 43, and 45 were amended to refer to the composition of claim 8 and directly incorporate the polypeptide immunogen description provided in a previous claim, rather than refer to a composition containing the polypeptide of a particular claim. For example, claim 37 was amended to directly provide the polypeptide immunogen description previously provided by reference to claim 3. The amendment was made to group the composition claims together rather than have a composition claim refer to a polypeptide claim.

Claims 38, 40, 42, 44 and 46 were amended to indicate the polypeptide immunogen is "substantially purified". Support for the amendment is provided on page 14, lines 23-30.

New claims 47 and 48 further describe the composition of claim 8. Support for claims 47 and 48 is provided, for example, by original claims 5 and 6, page 15, lines 1-7, along with the descriptions of "consists essentially" on page 13, lines 14-18.

New claims 49-54 further describe the immunogen of claim 7. Support for these claims is provided, for example, in the original claims and on page 12, line 33 to page 13, line 1.

Figure 1A was amended to provide a sequence identifier for the LPXTG motif; and to refer to amino acid # 609, instead of # 639. Support for the amendment is provided, for example, on page 8, lines 19-20 referring to a fragment from 461-609; SEQ ID NO: 3 providing a ORF0657nH region with an amino terminal methionine and 568 additional amino acid (569 total), which would correspond to ORF0657nH going from amino acid 42 to 609 in Figure 1A; and the present application at page 19, lines 9-10 pointing out ORF0657n contains a 36 amino acid C-terminal cell wall sorting sequence with a conserved "LPXTG" motif.

Objections to the Specification

The specification was objected to for failing to properly indicate trademarks, and not providing sequence identifiers for "LPXTG" in Figure 1A or for the sequence in Figure 1D. The specification was amended to capitalize trademarks noted by the examiner, to provide for some additional trademarks; and to provide the sequence identifier (SEQ ID NO: 42) in reference to Figure 1D. Figure 1A was amended to refer to "LPXTG" as SEQ ID NO: 109.

Claim Interpretation

In claim 5, reference to "consisting essentially" was interpreted to mean "comprising". Claim 5 was amended to replace "consisting essentially" with ". . . consisting. . . up to 20 additional amino acids, wherein the additional 20 amino acids can be located at the carboxyl or amino terminus."

Claims 2 and 3 were indicated to be confusing based on both open ended ("consists") and closed end ("comprising") language. As noted above, the claims were amended to more particularly describe "fragment thereof".

35 U.S.C. § 101

Claim 1-7 and 33-36 stand rejected for allegedly reading on a product of nature. The rejection indicates that corresponding polypeptides could be produced in nature through enzymatic truncation. Claim 1 was amended to indicate "purified" with respect to a polypeptide immunogen.

35 U.S.C. § 112, Second Paragraph (Definiteness)

The office action indicates that several claims are indefinite and provides suggestions for rendering some claims more definite.

(a) Claim 1 was indicated to be indefinite based on reference to "said polypeptide". The amendment to claim 1 includes the examiner's suggestion to reference "said polypeptide immunogen".

(b) Claims 2-6 were indicated to be indefinite for referring to "the polypeptide". Claims 3-6 were amended as suggested by the examiner to reference "polypeptide immunogen". Claim 2 was canceled and the description incorporated into claim 1 as discussed above.

(c) Claims 2 and 3 were indicated to be indefinite, confusing, and internally inconsistent based on reference to "said polypeptide consists of . . . a fragment . . . comprising". Claim 2 was canceled and the description incorporated into claim 1 as discussed above. Claim 3 was amended as discussed above.

(d) An analogous rejection and criticism was made to claim 7, as provided for in (c). As noted above, claim 7 was amended.

(e) Claim 7 was indicated to be indefinite and incorrect with respect to "regions moieties" and to lack antecedent basis for each region or moiety provided in line 4. Claim 7 was amended to clarify the objected to phrases.

(f) Claim 7 was indicated to be indefinite based on reference to additional "region or moiety". The examiner inquires whether a single amino acid would qualify. The claim indicates that the region or moiety has at least one of the following properties: enhances the immune response, facilitates purification, or facilitates polypeptide stability. A single amino acid having one of these properties would qualify. For example, an additional C- or N- terminal amino acid

can be present with a carboxyl or amino protecting group. (See, for example, the present application at page 14, lines 31-34.)

(g) Claim 1 was indicated to be indefinite based on reference to "one or more additional polypeptide regions". The amendment to claim 1 removes the objected to phrase.

(h) Claim 7 was indicated to be indefinite based on reference to "amino terminus". Claim 7 was amended as suggested by the examiner to indicate "the amino terminus".

(i) Claims 8, 37, 39, 43 and 45 were indicated to be vague based on reference to "induce an immune response in a patient". The office action indicates the specificity of the immune response in not clear, for example, is it directed to cancer, an autoimmune disease, AIDS, or a non-staphylococcal disease? Claim 8 previously referred to the immunogen of claim 1, where claim 1 described the immunogen as providing protective immunity to *S. aureus.* In addition, the claim 8 preamble was amended to indicate a protective immune response against *S. aureus.* Claims 37, 39, 43 and 45 were amended to depend from claim 8.

(j) Claims 2-6, 8, 9 and 33-46 were indicated to be indefinite based on their dependence from a claim identified in (a)-(i). The comments with respect to (a)-(i) are addressed above.

35 U.S.C. § 103(a)

Claims 1-8, 33-35, and 37-44 stand rejected as allegedly obvious in view of Foster *et al.* (US 6,841,154)('154) in view of Christensen *et al.* (US 7,456,276). Foster *et al.* ('154) is cited for describing a protein (KrkN) indicated to have a sequence identity of 100% to SEQ ID NO: 1, where the KrkN can allegedly be used to induce antibodies in a host animal, and be provided in a vaccine containing an immunogenically effective amount of the protein with a pharmaceutically acceptable carrier. Christensen *et al.* (US 7,456,276) is cited for attaching a His–Tag to the carboxyl terminus of an oligopeptide to facilitate purification. The rejection argues the skilled artisan would have been motivated to attach a His-Tag to the carboxyl end of the KrkN protein to facilitate protein purification, and that the produced protein would not have a carboxyl terminus containing amino acids 609-645 of SEQ ID NO: 2 due to the presence of the His-Tag. The rejection is respectfully traversed.

Claims 1, 5, 7, and 8 were amended as discussed above, so that the full-length ORF0657n sequence is not covered. Claims 3, 4, 6, 7, 33-35, and 37-44 as previously presented provided for less than the full-length sequence.

It is respectfully submitted that Foster *et al.* ('154) fails to provide a reasonable expectation of success, or even enable, using the KrkN protein or a shorter length version of the protein as a protective immunogen. Foster *et al.* ('154) appears to identify the KrkN protein based on a genomic analysis of *S. aureus* looking for open reading frames potentially coding for surface proteins with particular motifs. (See, for example, Foster *et al.* ('154) at column 3, line 21 to column 4, line 38.)

Foster *et al.* ('154) fails to provide any data concerning ability of the KrkN protein, or a structurally related sequence, to provide a protective immune response. Christensen *et al.* (US 7,456,276) is directed to peptide purification by means of metal ion affinity chromatography and does not cure the deficiencies of Foster *et al.* ('154).

Given that Foster *et al.* ('154) in combination with Christensen *et al.* (US 7,456,276) fails to provide a reasonable expectation that the full-length KrkN sequence is sufficient to provide a protective immune response, the skilled artisan would not have a reasonable expectation that shorter length derivatives would provide a protective immune response.

35 U.S.C. § 103(a)

Claim 9 stands rejected as allegedly obvious based on Foster *et al.* ('154) in view of Christensen *et al.* (US 7,456,276), and the art-known use of adding an adjuvant. The rejection is respectfully traversed.

As note above, claim 8 provides for a composition containing less than the full-length ORF0657n polypeptide. Claim 9 depends from claim 8. As noted in the previous section above, Foster *et al.* ('154) in view of Christensen *et al.* (US 7,456,276) does not make claim 8 obvious.

Claim Objections

Claim 37 was objected to for lacking a period at the end of the claim. The amendment to claim 37 provides a period.

Please charge deposit account 13-2755 for fees due in connection with this amendment. If any time extensions are needed for the timely filing of the present amendment, applicants petition for such extensions and authorize the charging of deposit account 13-2755 for the appropriate fees.

Respectfully submitted,

By /Sheldon O. Heber, Reg. No. 38,179/
Sheldon O. Heber
Reg. No. 38,179
Attorney for Applicants

Merck & Co., Inc.
P.O. Box 2000
Rahway, NJ 07065-0907
(732) 594-1958

APPENDIX